REMARKS

The Office Action of January 13, 2003 has been received and carefully considered. In response thereto, this Amendment has been submitted. It is submitted that, by this amendment, all bases of rejection and objection are traversed and overcome. Reconsideration is, therefore, respectfully requested.

The drawings are objected to as failing to comply with 37 C.F.R. 1.84(p)(5) because they include the following reference designations not mentioned in the specification. In Figure 3, these are reference numerals 28', 28", and 99. In Figure 5A, these are reference numerals 22, 60', 56, 50 and 42. The Examiner has required a proposed drawing correction, corrected drawings or amendment to the specification to add the reference designations in the description. These are required in the reply to the Office Action of January 13, 2003 to avoid abandonment of the application.

The specification has been amended in the following locations in response to the drawing objection. With regard to Figure 3, reference numerals 28' and 28" are present in ¶ 0045 as amended. Reference numeral 99 is present in ¶ 0047 as amended.

With regard to Figure 5A, reference numeral 60' is now present in ¶ 0059 as amended. Reference numeral 56 is present in ¶ 0058 as amended. Reference numeral 50 is present in ¶ 0057 as amended. Reference numeral 42 is present in ¶ 0056 as amended. Reference numeral 22 has been changed to reference numeral 28 in the drawing at Figure 5A. A proposed corrected drawing figure is being submitted with this amendatory response.

It is submitted that the proposed actions address and overcome the objections to the drawings. Furthermore, it is submitted that the drawings now comply with the provisions of 37 C.F.R. 1.84(p)(5).

Claim 4 currently stands rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner indicates that this is a written description rejection.

The Examiner indicates that claim 4 recites the defined volume of substances containing cellular material as comprising a plurality of individual volumes, wherein each individual volume is between about 1 and about 500 picoliters, and wherein characteristics of the substances continuing cellular material may vary from individual volume to individual volume in a known, predetermined manner. The Examiner indicates that the specification does not sufficiently teach that the defined volume would contain a plurality of individual volumes, wherein each individual volume is between and about 500 picoliters and wherein characteristics of the substances containing cellular material may vary from individual volume to individual volume.

The applicant respectfully submits that the specification includes the subject matter set forth in claim 4 as originally filed. Accordingly the applicant proposes amendment to ¶ 0065 as set forth on page 19. Claim 4 as originally filed is relied upon for support. Specifically, after the term "possible" in line 7 of ¶ 0065, the applicant proposes insertion of the phrase "that the individual volume is between about 1 and about 500 picoliters." Thus, the specific sentence as amended will read "It is also possible that the individual volume is between about 1 and about 500 picoliters, and that the content or specific characteristic of the substance containing cellular material may vary from individual volume to individual volume in a known predetermined manner." It is respectfully submitted that, in view of the proposed amendment, claim 4 now has appropriate written support within the description. Thus, it is submitted that claim 4 meets the requirements of 35 U.S.C. § 112, first paragraph.

Claims 1-10 currently stand rejected under 35 U.S.C. § 112, second paragraph, as failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Specifically, the examiner has indicated that the phrase "capturing data" is vague and indefinite because it is unclear how data can be captured since data are information that can be stored or collected by a computer or a mental process. Claim 1 has been amended deleting the phrase "capturing data". It is respectfully submitted that claim 1 as amended now comports with the requirement of 35 U.S.C. § 112, second paragraph.

Additionally, the term "known predetermined manner" in claim 4 is considered vague and indefinite because it is unclear what a "predetermined manner" is referring to. Claim 4 has been amended to address this issue. As a result of this amendment, it is submitted that claim 4 comports with the provisions of 35 U.S.C. § 112, second paragraph.

Claims 1-10 currently stand rejected under 35 U.S.C. § 102(b) as being unpatentable over the Stylli reference (U.S. Patent No. 5,985,214). The Examiner indicates that the Stylli reference teaches an automated method and system for identifying chemicals having useful activity such as biological activities and collecting information resulting from such process. The Examiner indicates that the method disclosed in Stylli comprises testing a therapeutic chemical for modulating activity of a target such as cell surface proteins in a cell-based assay. The Examiner also indicates that the method disclosed in Stylii comprises the step of dispensing the reagents into the addressable sample wells, which contain a predetermined volume of the sample or cellular material. For purposes of examination, the Examiner considers the reagents disclosed in Stylli to be equivalent to pharmacologically active agents. The electrically sensitive volume displacement unit disclosed in Stylli can dispense a predetermined volume of 1 to 500 picoliters. The wells are considered to be arranged in a two-dimensional array such as a 96-well plate. The method is considered to include storing, managing, and retrieving data collected from the assay process. The Examiner also indicates that the automated method can comprise multiple dispensers for dispensing different reagents in a complex screening process. Based upon this analysis, the Examiner concludes that the Stylli reference anticipates the presently claimed invention as set forth in claims 1-10.

Claim 1 currently stands rejected under 35 U.S.C. § 102(b) as being anticipated by the Stylli reference. The applicant's invention as set forth in claim 1 is directed to an automated method for analyzing substances containing cellular material. The method as set forth in claim 1 involves activating a test apparatus having at least one liquid ejection device. Support for the term "liquid ejection device" is found in the specification at ¶ 0039 line 2. The liquid ejection device acts in cooperation with an electronically activated printhead to dispense a first defined volume from the liquid ejection device into contact with at least one

defined volume of a substance containing cellular material. Support for the phrase "acting in cooperation with an electronically actuated printhead" is found at page 11, ¶ 0039, lines 12-14. It is submitted that the Stylli reference fails to teach or suggest the use of an apparatus having a liquid ejection device that acts in cooperation with an electronically activated printhead. Thus it is submitted that the applicant's invention as set forth in claim 1 is not taught, anticipated or rendered obvious by the Stylli reference.

The method also includes the step of detecting changes in the at least one defined volume of the substance containing cellular material triggered by introduction of the first defined volume of the potential pharmaceutically active agent. The method as set forth in claim 1 also includes the step of generating information indicative of an effect of the at least one potentially active agent on the cellular material and analyzing the generated information to generate a correlation factor. Support for the final two steps is found in Figure 1 and in the specification at page 8. Furthermore, it is submitted that the Stylli reference fails to teach or suggest the step of generating information indicative of an effect of the at least one potentially active agent and analyzing the generated information to generate a correlation factor. For these reasons, it is submitted that the applicant's invention as set forth in claim 1 is not taught, anticipated, or rendered obvious by the Stylli reference.

Claim 2 currently stands rejected under 35 U.S.C. § 102(b) as being anticipated by the Stylli reference. The applicant's invention as set forth in claim 2 is directed to an automated method in which the liquid ejection device comprises at least one cartridge containing at least one potential pharmaceutically active agent. The cartridge is removably associated with the liquid ejection device. It is respectfully submitted that Stylli does not teach the use of a removably associatable cartridge. Additionally claim 2 depends from claim 1 to contain all of the limitations found therein. By this dependency, it is submitted that the applicant's invention as set forth in claim 2 is not taught, anticipated, or rendered obvious by the sited reference for the reasons discussed previously in conjunction with claim 1.

Claims 3-9 currently stand rejected under 35 U.S.C. § 102(b) as being anticipated by the Stylli reference. Claims 3-9 depend either directly or

indirectly from claim 1 to contain all of the limitations found therein. By this dependency, it is submitted that the applicant's invention as set forth in claims 3-9 is not taught, anticipated, or rendered obvious by the sited reference for the reasons discussed previously in conjunction with claim 1.

Claim 10 also stands rejected under 35 U.S.C. § 102(b) as being anticipated by the Stylli reference. Claim 10 depends from claim 1 to specify that the method comprises a further step of interactively activating at least one second liquid ejection device to dispense a second defined volume of a potential chemically active substance into contact with the defined volume of the substance containing cellular material. It is submitted that the Stylli reference fails to teach or suggest the step of interactively activating at least one second liquid ejection device. For this reason and for the reasons discussed previously in conjunction with claim 1, it is submitted that the applicant's invention as set forth in claim 10 is not taught, anticipated, or rendered obvious by the Stylli reference.

Claims 1-10 currently stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Balch (US Patent 6,083,763) in view of Stylli (US Patent 5,985,214). The Balch reference is cited as disclosing a method of drug screening in which the drug to be screened reacts with biosite comprising biologically derived molecules deposited on the top surface of the substrate in a 96-well sample plate. The 96-well sample plate is scanned by a scanning mechanism to produce an image.

The Stylli reference is cited as teaching an automated method and system for identifying chemicals having useful activities such as biological activities and collecting information resulting from such a process. The Examiner cites the Stylli reference as comprising the step of testing a therapeutical chemical for modulating activity of a target such as cell surface proteins in a cell-based array. The method is also considered to comprise the step of dispensing reagents into addressable sample wells containing predetermined volumes of the sample. Electrically sensitive volume displacement unit can dispense predetermined volumes between 1 and 500 picoliters. The wells can be arranged in a two-dimensional array such as a 96-well plate. The method is also taken to include storing, managing and retrieving data collected from the assay process. The

Examiner concludes that the Stylli reference would provide the advantage of reducing the volume of sample processes and consumable cost.

The Examiner also indicates that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the method of dispensing drug onto the cellular material as taught by Stylli in the method of Balch. The Examiner concludes that one of ordinary skill in the art would have been motivated to include the method of dispensing drugs onto the cellular material in the method of Balch for the advantage of providing a reduction in the volume of sample processes and consumable costs as disclosed in Stylli.

The invention as presently claimed is directed to an automated method for analyzing substances containing cellular material. In the automated method, a test apparatus having at least one liquid ejection device acting in cooperation with an electronically activated printhead is activated to dispense a first defined volume into contact with a defined volume of a substance containing cellular material. The defined volume that is dispensed contains at least one potential pharmaceutically active agent.

The term "substance containing cellular material" as that term is employed in the claimed invention is defined as one which contains particular cells of interest for which evaluation of a potential pharmaceutically active material is sought (see page 9, ¶ 0035). The cells of interest are typically referred to as target cells. The process can be employed on biologically intact cells as well as on recognizable material from intact cells such as mitochondria, Golgi bodies, nuclei, nucleoli, and the like. Such materials suitable for testing and analysis by the method as set forth in claim 1 are those structures generally discernable by high resolution microscopy, including but not limited to, microscopic analysis such as scanning electron microscopy. The materials are those having measurable masses greater than molecular levels (see page 10, ¶ 0037).

In contrast, the Balch reference is directed to testing of "biosite" material. The Balch reference defines such material as biological molecules or capture probes that are deposited on the top surface of the reaction substrate or base material. The Balch reference fails to teach or suggest a test method that can be employed on samples containing intact cells and/or recognizable material from intact cells having measurable masses greater than molecular levels. In

contrast, the Balch reference is directed to a method of molecular analysis. It is respectfully submitted that the Balch reference fails to teach or suggest a method in which potential pharmaceutically active agents could be evaluated by detecting changes in the defined volume of the substance containing cellular material and generating information indicative of the observed effect and analyzing the generated information to generate a correlation factor.

The Stylli reference lacks any teaching which would suggest dispensing of material from at least one liquid ejection device acting in cooperation with an electronically activated printhead. It is submitted that the ejection method defined in claim 1 provides accuracy, reproducibility, and, when necessary, variability not taught or suggested in the Stylli reference or the Balch reference, taken alone or in combination. Furthermore, it is submitted that the references fail to teach or suggest a step in which information indicative of the effect of at least potential pharmacologically active agent on cellular material is generated and the analysis of such generated information to develop a correlation factor occurs. For these reasons, it is submitted that the applicant's invention as set forth in claim 1 is not taught, anticipated, or rendered obvious by the cited references.

Claim 2 currently stands rejected under 35 U.S.C. § 103(a) as being rendered obvious by Balch in view of Stylli. The applicant's invention as set forth in claim 2 is directed to an automated method in which the liquid ejection device comprises at least one cartridge containing at least one potential pharmaceutically active agent. The cartridge is removably associated with the liquid ejection device. It is respectfully submitted that neither Balch nor Stylli teach the use of a removably associatable cartridge. It is contemplated that appropriate removable cartridges can be utilized to accomplish various challenge tests for various materials to readily and efficiently ascertain efficacy of various materials or standards suitable packaged in the removable cartridge. Additionally, claim 2 depends from claim 1 to contain all of the limitations found therein. By this dependency, it is submitted that the applicant's invention as set forth in claim 2 is not taught, anticipated, or rendered obvious by the cited references.

Claims 3-5, 8, and 9 also stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by Balch in view of Stylli. The applicant's invention as

set forth in claims 3-5, 8, and 9 depends either directly or indirectly from claim 1 to contain all of the limitations found therein. By this dependency, it is submitted that the applicant's invention as set forth in claims 3-5, 8 and 9, is not taught, anticipated, or rendered obvious by the cited references for the reasons discussed previously in conjunction with claim 1.

Claim 6 currently stands rejected under 35 U.S.C. § 103(a) as being rendered obvious by Balch in view of Stylli. The applicant's invention as set forth in claim 6 includes the limitation that the at least one liquid ejection device dispenses a quantity of at least one potential pharmaceutically active agent into contact with selected individual volumes containing cellular material. The dispensed quantity varies compositionally across the individual volumes of the substance containing cellular material. It is respectfully submitted that the Balch and Stylli references fails to teach or suggest at least one liquid ejection device which dispenses a quantity of at least one potential pharmaceutically active agent into contact with selected individual volumes in a manner that varies compositionally across the individual volumes containing cellular material. Additionally, claim 6 depends ultimately from claim 1 to contain all of the limitations found therein. By this dependency, it is submitted that the applicant's invention as set forth in claim 6 is not taught, anticipated, or rendered obvious by the cited references for the reasons discussed previously in conjunction with claim 1.

Claim 7 also stands rejected under 35 U.S.C. § 103(a) as being rendered obvious by Balch in view of Stylli. The applicant's invention as set forth in claim 7 is directed to an automated method in which the defined volume of the substance containing cellular material is present as a plurality of individual samples arranged in an array capable of yielding statistically viable data. It is submitted that the Balch reference fails to reach or suggest a method whereby a volume of a substance containing cellular material as defined in the present invention is present as a plurality of individual samples arranged in an array. It is submitted that the Stylli reference fails to teach or suggest dispensing a material from an ejection device having an electronically activated printhead into the volume present as a plurality of individual samples arranged as an array. Furthermore, It is respectfully submitted that claim 7 depends from independent

claim 1 to contain all of the limitations found therein. By this dependency, it is submitted that the applicant's invention as set forth in claim 7 is not taught, anticipated, or rendered obvious by the cited references.

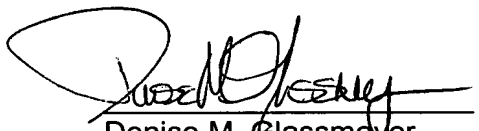
Claim 10 also stands rejected under 35 U.S.C. § 103(a) as being rendered obvious by Balch in view of Stylli. The applicant's invention as set forth in claim 10 is directed to a method which includes the step of interactively activating at least one second liquid ejection device to dispense a second defied volume of a potential pharmaceutically active agent into contact with the defined volume of the substance containing cellular material. It is respectfully submitted that the Balch and Stylli references fail to teach or suggest the dispensing of at least one second liquid into contact with the substance containing cellular material. It is respectfully submitted that the interactive and sequential dispensing of multiple materials, in combination with the generation of information and analysis permits analytical flexibility and greater complexity in analytical design. Without being bound to any theory, it is believed that administration of materials from at least one liquid ejection device having an electronically actuated printhead permits effective introduction of material into samples containing intact cells or cellular organelles in a manner which permits observation of responses and the interactive activation of at least one second liquid ejection device. Thus, it is submitted that the Stylli and Balch references fail to teach or suggest such features. Thus, it is submitted that the applicant's invention as set forth in claim 10 is not taught, anticipated, or rendered obvious b the cited references.

In summary, claims 1, 2, 4, 5, 10 have been amended. Additionally, discussion has been presented as to why the applicant's invention as set forth in claims 1-10 is not taught, anticipated, or rendered obvious by the cited references. In view of this amendment and the foregoing discussion, it is submitted that the applicant's invention as set forth in claims 1-10 is in a condition suitable for allowance, a notice of which is respectfully requested.

New claims 27-35 have been added by this action. Support for new claim 27 is found in claim 19 as originally presented. Support for claim 28 is found in originally presented claim 21. Claim 29 has been added to provide for positioning of cellular material substance on a substrate. Support is inferred from claim 3. Support for claim 30 is found in claims 4 and 7.

Support for newly presented claims 31 and 32 is found in claims 25 and 26 as originally presented. Support for claim 33 is found in claim 4. Support for claims 34 and 35 is found in claims 8 and 9. Entry and favorable consideration of claims 27-35 is respectfully requested.

Respectfully submitted,



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